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Pharyngeal airway dimensions: a cephalometric, growth-study-based analysis of physiological variations in children aged 6-17

Mislik, Barbara ; Hänggi, Michael P ; Signorelli, Luca ; Peltomäki, Timo A ; Patcas, Raphael

Abstract: OBJECTIVE:The aim was to assess pharyngeal airway dimensions and physiological changes based on lateral cephalometric radiographs from healthy untreated children aged 6-17 years.MATERIALS/METHODS:The sample consisted of 880 lateral cephalograms (412 females and 468 males) of the Zurich Craniofacial Growth Study. Statistical analyses on cephalometric measurements of airway dimensions (distances 'p': shortest distance between soft palate and posterior pharyngeal wall and 't': shortest distance between tongue and posterior pharyngeal wall) and craniofacial parameters were performed. To disclose differences between different age groups, a Kruskal-Wallis test was applied. The influence of gender on 'p' and 't' was analysed by a Mann-Whitney U-test for each age group separately. The Spearman correlation was computed in order to investigate associations between craniofacial parameters. Variables associated with 'p' and 't' were chosen for multiple regression model investigation.RESULTS:The results demonstrated high interindividual variations. A slight influence of age on 'p' ($P = 0.034$) could be attested (+1.03mm) but not on 't' ($P = 0.208$). With the exception of the 9-year age group, no significant differences between the genders were found. Correlation analysis revealed several statistically significant correlations between 't' or 'p' and antero-posterior cephalometric variables. All correlation coefficients were, however, very low and the adjusted coefficient of determination also revealed the regression model to be very weak.CONCLUSIONS:The high interindividual variations of 'p' and 't' render the use of reference values problematic. Contrary to other craniofacial structures, neither age-related changes nor sexual dimorphism were found for 'p' and 't'. Any associations to antero-posterior cephalometric characteristics seem low.

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Summary (250 words)

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Materials/Methods: The sample consisted of 880 lateral cephalograms (412 females; 468 males) of the Zurich craniofacial Growth study. Statistical analyses on cephalometric measurements of airway dimensions (distances “p”: shortest distance between soft palate and posterior pharyngeal wall and “t”: shortest distance between tongue and posterior pharyngeal wall) and craniofacial parameters were performed. To disclose differences between different age groups, a Kruskal-Wallis test was applied. The influence of gender on “p” and “t” was analysed by a Mann-Whitney-U-test for each age group separately. The Spearman correlation was computed in order to investigate associations between craniofacial parameters. Variables associated with “p” and “t” were chosen for multiple regression model investigation.

Results: The results demonstrated high interindividual variations. A slight influence of age on “p” ($p=0.034$) could be attested (+1.03mm), but not on “t” ($p=0.208$). With the exception of the 9-years-age-group, no significant differences between the genders were found. Correlation analysis revealed several statistically significant correlations between “t” or “p” and antero-posterior cephalometric variables. All correlation coefficients were, however, very low and the adjusted coefficient of determination also revealed the regression model to be very weak.

Conclusions: The high interindividual variations of “p” and “t” render the use of reference values problematic. Contrary to other craniofacial structures, neither age-related changes nor sexual dimorphism were found for “p” and “t”. Any associations to antero-posterior cephalometric characteristics seem low.

Introduction

Interest in upper airway shape and dimensions has increased steadily during the past few decades, mainly due to the appreciation of the relationship between upper airway configuration and sleep-disordered breathing (SDB) as well as its relation to craniofacial morphology in general (Guijarro-Martinez and Swennen, 2011; Katyal *et al.* 2013; Flores-Mir *et al.*, 2013).

SDB refers to a wide variety of breathing anomalies ranging from chronic or habitual snoring to upper airway resistance syndrome (UARS) and to obstructive sleep apnea (OSA). SDB mostly results from a combination of anatomic factors that predispose the airway to collapse during inspiration, combined with an insufficient neuromuscular compensation during sleep to maintain airway patency (Young *et al.*, 2002). Among anatomic factors adenotonsillar hypertrophy is considered to be the most commonly recognized cause for SDB in children (Marcus 2000). Deviant craniofacial morphology is also a predisposing factor (Pirilä-Parkkinen *et al.*, 2010; Katyal *et al.*, 2013).

SDB is associated with several symptoms in children, the severity of which varies according to the severity of the disorder. Snoring, enuresis, frequent episodes of hypoxia and awakenings are common night-time symptoms and consequences, which disrupt continuous sleep and can cause significant daytime problems (Young *et al.*, 2002). Excessive sleepiness, decrease in school performance, abnormal behavior, growth disturbance and the progressive development of hypertension are frequently found. An association between SDB, sleep bruxism and headache has also been reported in children and adolescents (Carra *et al.*, 2012).

Early diagnosis of SDB is imperative in order to promote normal facial development (Peltomäki 2007; Aboudara *et al.*, 2009). Small pharyngeal dimensions

established early in life may predispose to later SDB or even to OSA (Papaioannou *et al.*, 2013), when subsequent soft tissue changes caused by normal ageing, obesity or genetic background further reduce the patency of the oropharynx (Martin *et al.*, 1997).

First and foremost sign of SDB are pathologic breathing and sleeping pattern, which may be evaluated and recorded in the patient's history. Lateral cephalograms have, to no little extend, also been used to diagnose restricted dimensions of the oropharynx (Battagel *et al.*, 2000; Kuhnel *et al.*, 2005), identifying certain decreased pharyngeal dimensions characteristic to OSA (Battagel and L'Estrange, 1996). In a systematic review, lateral cephalometry has been found to be a reliable initial screening tool of upper airway obstruction to determine the need for more in-depth ENT follow-up (Major *et al.*, 2006).

Literature on physiologic airway dimensions in growing subjects is however scarce and, in case a reference value was needed, most studies compared airway dimensions of SDB subjects to a relative small control group. These comparative studies have found airway dimension to average 10-12 mm at its shortest distance between the tongue and the posterior pharyngeal wall and 9-10mm at its shortest distance between the soft palate and the posterior pharyngeal wall. (de Freitas *et al.*, 2006; Hanggi *et al.*, 2008; Pirilä-Parkkinen *et al.*, 2011; Bollhalder *et al.*, 2012). Yet little is known about the development of airway dimensions in healthy children and if age or gender have an influence on airway dimensions.

The aim of this retrospective cross-sectional study was to evaluate pharyngeal airway dimensions and their physiological changes based on a large sample size of lateral cephalograms of healthy untreated children between 6 and 17 years of age. To our knowledge, no previous attempt has been made so far to study airway dimensions from a large sample, enabling to classify all measurements according to age and

gender.

Material and Methods

Subjects

The lateral cephalograms used for this study were derived from the Zurich Craniofacial Growth Study performed in the years 1981-84 at the Department of Orthodontics and Paediatric Dentistry of the University of Zurich. In the original study, 884 healthy schoolchildren of Caucasian ethnicity from all local public schools of the city of Zurich with no history of orthodontic treatment were randomly selected and examined. Based on a health questionnaire, subjects with severe systemic diseases and children under medication were excluded from the selection. Different skeletal or dental malocclusions as well as breathing pattern, habits, enlarged tonsils, snoring etc. were not considered as exclusion criteria.

The examination always took place very close to the individual's birthday. Ethical and legal approval for releasing the data was obtained by the Federal Commission of Experts for Professional Secrecy in Medical Research (Federal Authorities of the Swiss Confederation 2011). All cephalograms utilized for this study had to be of good quality and the airway had to be clearly visible. Thus, the final sample used consisted of 880 cephalograms (412 females, 468 males. The gender distribution for all ages is given in Tables 2A and 2B).

Methods

All cephalograms were taken with the same custom-made x-ray device (COMET, 3175 Flamatt, Switzerland) in a standardized position: The teeth were in centric occlusion, the head was aligned with the Frankfort horizontal plane parallel to

the floor. This position was stabilized with ear rods and a nasal support to prevent the head from rotating during exposure. The focus-coronal plane distance was 200cm, film-coronal plane distance was 15cm and the magnification was 7.5%.

The subjects were asked to refrain from swallowing during the radiological examination. Tongue posture was subsequently assessed on the cephalograms to ascertain that the children did not swallow.

Three investigators who had been calibrated previously by a board-certified orthodontist, traced and landmarked the lateral cephalograms by hand according to the definitions listed in Table 1 and shown in Figure 1. The digitizing was performed using a tablet digitizer (NumonicsAccuGrid, Lansdale, Pennsylvania, USA) with a resolution of 1milli-Inch. The digitized cephalometric values were calculated using self-written software.

For the assessment of the dimension of the airway, two distances were evaluated as described in other airway studies (McNamara, 1984; Rodenstein *et al.*, 1990; Finkelstein *et al.*, 2001; Pirila-Parkkinen *et al.*, 2011; Alves *et al.*, 2012): distance “p”, as the shortest distance between the soft palate and the posterior pharyngeal wall, and distance “t” as the shortest distance between the tongue and the posterior pharyngeal wall.

In addition to the conventional measurements of for pro- and retrognathism (SNA, SNB), distance ratios were also introduced. Three distances parallel to the Frankfort horizontal plane, perpendicular to a vertical line through Sella (point S), were measured to Nasion (point N), point A and point B, respectively (Figure 1B). Subsequently, three ratios were defined as: distance to point A / distance to point N (“ratio A/N”), distance to point B / distance to point N (“ratio B/N”), distance to point [(A+B)x0.5] / distance to point N (“ratio AB/N”).

38 cephalograms were traced a second time more than 6 months apart, 19 by the same investigator and 19 by a different investigator, in order to determine intra- and interobserver reproducibility.

Statistical methods

The data were analysed with SPSS (IBM SPSS version 20, Armonk, New York, U.S.A.). To determine intra- and interobserver reliability, the intraclass correlation coefficient (ICC) for absolute agreement based on a one-way random effects analysis of variance (ANOVA) was calculated.

Descriptive statistics were computed for all variables of interest for each age group separately. The distances “p” and “t” were tested for normal distribution using the tests of Kolmogorov-Smirnov and Shapiro-Wilk, revealing that “p” and “t” differ statistically significantly from normal distribution. Therefore, non-parametric tests were used for further investigations.

The association between age and distances “p” and “t” were investigated graphically and a non-parametric estimate of the mean influence was provided by the Loess-smoother (Cleveland and McGill, 1985), in order to visualize the dependency of “p” and “t” to age. Kruskal-Wallis test was applied to disclose the differences in mean values of “p” or “t” between the age groups.

The influence of gender on distances “p” and “t” was analysed by a Mann-Whitney-U-test for each age group separately.

~~The~~ Spearman correlation was computed in order to investigate associations between distances “p” and “t” and cephalometric parameters. Additionally, partial parametric correlations were performed to adjust for multiple correlations due to age, gender and all cephalometric predictors used. Variables that showed tendencies for associations with distances “p” and “t” ($p < 0.1$) were chosen for multiple regression

model investigations. Backward search procedure was applied in order to obtain the most parsimonious model. The resulting optimal multiple linear regression model was refitted again using the entire procedure. The estimates of the adjusted regression coefficient and the corresponding p-values were provided. The relevance of the model was discussed according to the adjusted R^2 -statistic.

Results of statistical analysis with p-value smaller than 0.05 were considered to be statistically significant.

Results

The ICC revealed a very good repeatability for all cephalometric measurements. The mean value for all measurements was 0.948 (1.SD: 0.142; Min.: 0.729; Max.: 0.995) for intraobserver repeatability and 0.933 (1.SD: 0.141; Min.: 0.700; Max.: 0.996) for interobserver repeatability, respectively. These ICC values are comparable to other airway studies (Bollhalder *et al.*, 2012) and indicate a reliable reproducibility of the measurements.

The distributions of airway distances “p” and “t” corresponding to the age of the subjects are shown graphically in Figure 2 and Figure 3, respectively. The mean distances and standard deviation for distance “t” and “p” are presented in Tables 2A and 2B. Both tests for normality revealed that distances “t” and “p” differ statistically significantly from normal distribution (Kolmogorov-Smirnov for “t”: 0.000 and “p”: 0.000; Shapiro-Wilk for “t”: 0.000 and “p”: 0.010), and hence, non-parametric tests were used for further investigations.

The Kruskal-Wallis test on all 880 subjects revealed a statistically significant influence of age on distance “p” ($p=0.034$), but no impact on distance “t” ($p=0.208$). This association with “p” can also be seen when comparing Figure 2 and Figure 3.

The Loess interpolation line shows in Figure 2 a slight, but continuous increase of “p” of about 1.03 mm over the 11-year period. In Figure 3 the Loess interpolation line demonstrates that “t” decreases slightly between 6 and 12 years of age, and then increases again up to 17 years of age.

The investigation on the association of gender to distances “t” and “p” found no important influence. Only in the 9-years-age-group significant differences between the genders for distances “t” (p-value 0.009) and “p” (p-value 0.002) were found. The statistical results are given in Tables 3A and 3B for distances “p” and “t”, respectively.

The Spearman correlation analysis revealed several statistically significant correlations between the distances “t” and “p” and cephalometric parameters. The results of the correlation analysis, including the partial parametric correlation analysis adjusted for age, gender and predictors, are presented in Table 4. Significant positive correlations for distance “t” and “p” were found with the cephalometric values of ratio B/N, ratio A+B/N, SNA, SNB and a significant negative correlation with NS/Gn. For distance “p”, a further negative correlation with SpaSpp/MGo was observed. The two last parameters (NS/Gn and SpaSpp/MGo) did, however, not correlate significantly when adjusted for age, gender and the other parameters. Moreover, all mentioned significant correlations had small correlation coefficients, and it is remarkable that no correlations to ANB were found, neither for distance “t”, nor for distance “p”.

Variables that showed statistical tendencies ($p < 0.1$) or associations with distance “p” and distance “t” were chosen for multiple regression model investigations. These are presented in Table 5A for distance “t” and Table 5B for distance “p”, with the possible variables listed for “t” and “p” separately. The adjusted Coefficient of determination (R^2) of the multiple linear regressions-model was 0.18

for distance “p” and 0.31 for distance “t”, indicating the inherent insufficiency of the model to adequately predict “p” or “t”.

Discussion

Rationale behind this study and the parameters used

This study investigated the pharyngeal airway dimensions based on 880 lateral cephalometric radiographs from healthy, orthodontically untreated children aged 6 to 17 years. It is the first attempt to establish reference values of airway dimensions based on a large growth study.

Limitations of lateral cephalometry in airway studies have been discussed (Lowe *et al.*, 1986; Battagel and L'Estrange, 1996; Finkelstein *et al.*, 2001), particularly the inadequate representation of upper airway structures in a two-dimensional radiograph. Information is obviously lost on the transverse airway dimension, and its value as a diagnostic tool has been questioned, as a solid assessment of airway dimensions would require a three-dimensional imaging technique such as computerized tomography or magnetic resonance imaging (Lowe *et al.*, 1986; Rodenstein *et al.*, 1990).

The upper airway is not a rigid structure and its dimensions are influenced by many factors. These include supine or upright positioning, awake or asleep muscle tone, inspiration or expiration, duration of x-ray exposure and mouth opening. Considering these circumstances, it becomes evident that even a three-dimensional radiographic representation does not account for the true clinical circumstances under which SDB and particularly OSA may occur.

In a 3D CBCT study comparing OSA to non-OSA patients, only the smallest cross-section airway area was found to be significantly different between the two

groups (Ogawa *et al.*, 2007). Hence, only the smallest cross-section airway area, i.e. the anterior-posterior dimension, seems to be of clinical relevance. This observation was recently substantiated by another study demonstrating lateral cephalogram to be a valid imaging method and a good screening tool when compared to MRI: the measuring dimensions of the nasopharyngeal and retropalatal region in children correlated significantly to MRI findings, and both techniques revealed the narrowest measurement to be the anterior-posterior distance located in the retropalatal region (Pirilä-Parkkinen *et al.*, 2011). Finally, a systematic review concluded that lateral cephalometrics can be considered a reliable initial screening tool of upper airway obstruction (Major *et al.*, 2006). It is safe to presume that although an airway assessment based on cephalograms will be limited on a two-dimensional depiction of the airway, it nevertheless will represent the critical and pivotal distances for airway patency. Conventional lateral cephalogram remains therefore not only a solid and routine diagnostic tool for orthodontics, but also a legitimate instrument for airway measurements (Aboudara *et al.*, 2009).

Distances “t” and “p” and the influence of age

In the present study the smallest distance from soft palate to the posterior pharyngeal wall, i.e. distance "p", known also as McNamara's line was used. Even though no consensus exists concerning the measurements of the nasopharynx, this distance is the only one with some validation from multiple studies (Major *et al.*, 2006). Dimension "t" on the other hand is the most widely used measurement of the retroglossal dimension.

The measurement results of distances “p” and “t” show high interindividual variations, but only small differences between the different age groups. The individual

variation of the parameters measured is substantial enough to render the use of mean values, when applied to individual cases, as questionable.

This study illustrates that distance “t” decreases slightly between 6 and 12 years of age, and then increases slightly up to 17 years of age. The results for distance “t” are in agreement with earlier studies (McNamara, 1984; Ogawa *et al.*, 2007; Hanggi *et al.*, 2008; Alves *et al.*, 2012). The observed initial decrease of “t” could probably be attributed to the distinct growth pattern of the tongue, which resembles neural growth pattern. Thus, during the juvenile phase, tongue growth will be more intense compared to the growth of all its surrounding structures, which follow visceral growth pattern. It is this disparity that possibly causes the initial decrease of distance “t”. Distance “p” displayed a slight continuous increase of about 1.03 mm between 6 and 17 years of age. This increase is also confirmed by McNamara (1984) and is probably related to the decline of the adenoid size during this growth period. However, caution should be applied when interpreting the small yet statistically significant age-related increase, as a large interindividual distribution, which can be observed similarly for both airway measurements, is very apparent.

Considering how abundant craniofacial growth and development is between 6 to 17 years of age, it is contrary to expectation that no radical change in the upper airway dimensions were found. It seems that the upper airway dimensions are formed and matured in the early periods of growth, and those years seem to be of high relevance to ensure the later physiological need of an adequate airflow.

Influence of gender and cephalometric variables on distances “t” and “p”

Sexual dimorphism in craniofacial dimensions is a fact that has been established in various analyses (Schudy, 1965; Bishara and Jakobsen, 1985; Siriwat and Jarabak,

1985; Nanda, 1988). Yet, maybe surprisingly, there were no differences in airway dimensions of distance “t” and “p” between male and female subjects. In general, females are smaller in stature than men (having less muscle mass and smaller heads) and subsequently require less oxygen. If airways in women are of similar dimensions to those in men, it follows that their airways must be larger in relative terms and this may be one of the reasons that women would be less prone to OSA than men. Further studies are, however, needed to substantiate this hypothesis. It may be of importance that females have smaller cross-sectional area of the tongue than males measured from lateral cephalograms, and that females reach adult values earlier (Cohen and Vig, 1976). One may question the validity of cephalometric measurements on tongue size, but a highly significant correlation has been found between lingual volume measured on MRI and the area of the lingual shadow measured on profile radiographs (Liegeois et al., 2010).

Only few and weak correlations of “p” and “t” to the cephalometric landmarks were found. In fact, no correlations were found to otherwise important variables such as the angle of the mandible or skeletal class (e.g. ANB or WITS). A significant, however weak, correlation could be established to the pro- and retrognathism of the maxilla and mandible and to the Y-axis.

The evaluated coefficient of determination R^2 for the regression-models for distance “p” and “t” respectively indicates that the established model will not fit any future data very well. This corroborates the observation that associations between airway dimensions and other craniofacial measurements are weak, and is partly contrary to other studies (Abu Allhaija and Al-Khateeb, 2005; Alves *et al.*, 2012).

Conclusion

Based on the data of the examined population, the following observation can be made: The mean value of distance “p” increases continuously from age 6 (8.12mm) to age 17 (9.15mm). The mean value of distance “t” decreases from age 6 (10.61mm) to age 10 (9.31mm), but increases afterwards again up to age 17 (11.19mm). However, both distances “p” and “t” show high interindividual variations and render the use of a mean value as reference on individuals questionable. Small differences between the different age groups could be observed, but no differences between the genders. Only weak correlations of distances “p” and “t” to certain cephalometric landmarks were found, but no correlation with ANB. The results show that upper airway dimensions in growing children from 6 to 17 years of age remain remarkably stable on average and suggest that the airway dimensions are being established in early childhood.

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Figure Legends

Figure 1. Cephalometric points and pharyngeal distances used in this study: Distance “p” and “t”. New cephalometric distances introduced (thick black lines): Distance to N, A and B. All distances are measured to a line through S, perpendicular to the Frankfort horizontal plane.

Figure 2. Graphical distribution of airway distance “p” corresponding to the age of the subjects (n=880) and Loess interpolation line.

Figure 3. Graphical distribution of airway distance “t” corresponding to the age of the subjects (n=880) and Loess interpolation line.